

AMENDMENTS

In the Claims

1.(canceled)

2.(canceled)

3.(canceled)

4.(canceled)

5.(canceled)

6.(canceled)

7.(canceled)

8.(canceled)

9.(canceled)

1 10.(allowed) A composition comprising a polymerizing agent including a molecular and/or atomic
2 tag covalently bonded to a site on the polymerizing agent and a monomer including a molecular
3 and/or atomic tag, where at least one of the tags has a fluorescence property that undergoes a change
4 before, during and/or after each of a sequence of monomer incorporations due to an interaction
5 between the polymerizing agent tag and the monomer tag and where the changes in the detectable
6 property generate data evidencing each monomer incorporation producing a monomer sequence read
7 out.

1 11.(allowed) The composition of claim 10, wherein the change in the fluorescence property results
2 from a change in the conformation of the polymerizing agent from a first conformational state to a
3 second conformational state and back again during each monomer incorporation.

1 12.(allowed) The composition of claim 10, wherein the fluorescence property has a first detection
2 propensity when the polymerizing agent is in the first conformational state and a second detection
3 propensity when the polymerizing agent is in the a second conformational state.

1 13.(allowed) The composition of claim 12, wherein the polymerizing agent is a polymerase or
2 reverse transcriptase.

1 14.(allowed) The composition of claim 13, wherein the polymerase is selected from the group

consisting of *Taq* DNA polymerase I, T7 DNA polymerase, Sequenase, and the Klenow fragment from *E. coli* DNA polymerase I.

15.(allowed) The composition of claim 13, wherein the reverse transcriptase comprises HIV-1 reverse transcriptase.

16.(allowed) The composition of claim 12, wherein each of the monomers comprises a deoxynucleotide triphosphate (dNTP) and the monomer tag is covalently bonded to the β or γ phosphate group of each dNTP.

17.(allowed) The composition of claim 10, wherein the tags comprise fluorescent tags and the fluorescence property comprises an intensity and/or frequency of emitted fluorescent light.

18.(currently amended) The composition of claim 17, wherein the fluorescentce property is fluorescence resonance energy transfer (FRET) where either the monomer tag or the polymerase tag comprises a donor and the other tag comprises an acceptor and where FRET occurs when the two tags are in close proximity.

19.(currently amended) The composition of claim 14, wherein the polymerase comprises *Taq* DNA polymerase I having a tag attached at a site selected from the group consisting of 513-518, 643, 647, 649 and 653-661 ~~and mixtures or combinations thereof~~ of the *Taq* polymerase, where the tag comprises a fluorescent molecule.

20.(canceled)

21.(canceled)

22.(canceled)

22.(canceled)

23.(canceled)

24.(canceled)

25.(withdrawn) A single molecule sequencing apparatus comprising a substrate having a first chamber in which at least one tagged polymerase is confined therein and a second chamber

including tagged dNTPs and a channel interconnecting the chambers, where a detectable property of at least one tag undergoes a detectable change during a monomer incorporation cycle.

1 26.**(withdrawn)** The apparatus of claims 24, further comprising a plurality of monomer
2 chambers, one for each tagged dNTP.

1 27.**(withdrawn)** A mutant Taq polymerase comprising native Taq polymerase with a cysteine
2 residue replacement at a site selected from the group consisting of 513-518, 643, 647, 649 and 653-
3 661 and mixtures or combinations thereof.

1 28.**(withdrawn)** The polymerase of claim 27, wherein the cysteine residue includes a tag
2 covalently bonded thereto through the SH group.

1 29.**(withdrawn)** A system for retrieving stored information comprising:
2 a unknown nucleotide sequence representing a data stream;
3 a single-molecule sequencer including a polymerase having a tag associated therewith and
4 monomers for the polymerase, each monomer having a tag associated therewith;
5 an excitation source adapted to excite the at least one of the tags; and
6 a detector adapted to detect a response from at least one of the tag,
7 where the response changes during polymerization of a complementary sequence and the
8 changes in response represent a content of the data stream.

1 30.**(withdrawn)** A system for determining sequence information from a single molecule
2 comprising:
3 a unknown nucleotide sequence;
4 a single-molecule sequencer comprising a polymerase having a tag associated therewith and
5 monomers for the polymerase, each monomer having a tag associated therewith;
6 a excitation source adapted to excite at least one of the tags; and
7 a detector adapted to detect a response from at least one of the tags,
8 where the response changes during polymerization of a complementary sequence and the
9 changes in the response represent the identity of each nucleotide in the unknown sequence.

1 31.(withdrawn) A method for sequencing a molecular sequence comprising:
2 supplying an unknown sequence of nucleotides or nucleotide analogs to a single-molecule
3 sequencer comprising a polymerase having a fluorescent donor covalently attached thereto and
4 monomers for the polymerase, each monomer having a unique fluorescent acceptor covalently
5 bonded thereto;
6 exciting the fluorescent donor with a light from an excitation light source;
7 detecting emitted fluorescent light from the acceptor during a monomer incorporation cycle
8 via a fluorescent light detector, where an intensity and/or frequency of the emitted light for the
9 acceptors changes during each monomer incorporation cycle; and
10 converting the changes into an identity of each nucleotide or nucleotide analog in the
11 unknown sequene.

1 32.(withdrawn) A method of sequencing an individual nucleic acid molecule or numerous
2 individual molecules in parallel including the steps of:
3 immobilizing a member of the replication complex comprising a polymerase including a tag
4 attached thereto, a primer or a template sufficiently spaced apart to allow resolution detection of
5 each complex on a solid support;
6 incubating the replication complex with cooperatively-tagged nucleotides, each nucleotide
7 including a unique tag at its gamma-phosphate, where each nucleotide can be individually detected;
8 detecting each nucleotide incorporated by the polymerase as the polymerase transitions
9 between its open and closed form, which causes a change in a detectable property of at least one of
10 the tags or as the pyrophosphate group is released by the polymerase; and
11 relating the changes in the detectable property to the sequence of nucleotides in an unknown
12 nucleic acid sequence.

1 33.(withdrawn) A γ -phosphate modified nucleoside comprising γ -phosphate modified dATP,
2 dCTP, dGTP and dTTP.

1 34.(withdrawn) A primer sequence or portion thereof selected from the group consisting of
2 Sequence 1 through 29.

35.(canceled)

36.(canceled)

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40.(canceled)

41.(canceled)

42.(canceled)

43.(canceled)

44.(canceled)

45.(canceled)

46.(canceled)

47.(canceled)

1 48.(new) A composition comprising a polymerizing agent including at least one molecular
2 and/or atomic tag covalently bonded to a site on the polymerizing agent, where a fluorescence
3 property of the tags undergoes a change before, during and/or after each of a sequence of monomer
4 incorporations and where the changes in the fluorescence property generate data evidencing each
5 monomer incorporation producing a monomer incorporation read out and where the polymerizing
6 agent comprises a *Taq* DNA polymerase I having a tag covalently bonded to an amino acid site of
7 the *Taq* polymerase selected from the group consisting of 513-518, 643, 647, 649 and 653-661 and,
8 where the tag comprises a fluorescent molecule.

1 49.(new) The composition of claim 48, wherein the fluorescence property has a first value
2 when the polymerizing agent is in a first state and a second value when the polymerizing agent is
3 in a second state, and where the polymerizing agent changes from the first state to the second state
4 and back again during each monomer incorporation.